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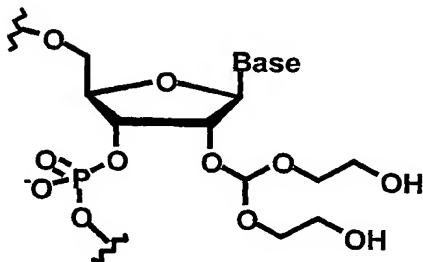
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(54) Title: MODIFIED POLYNUCLEOTIDES FOR USE IN RNA INTERFERENCE



Structure of 2'-ACE protected RNA.

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(57) **Abstract:** Methods and compositions for performing RNA interference comprising a wide variety of stabilized siRNAs suitable for use in serum-containing media and for in vivo applications, such as therapeutic applications, are provided. These siRNAs permit effective and efficient applications of RNA interference to applications such as diagnostics and therapeutics through the use of one or more modifications including orthoesters, terminal conjugates, modified linkages and 2'-modified nucleotides. Uniquely modified siRNAs have been developed that reduces off-target effects incurred in gene-silencing. The modifications include phosphorylation of the first 5' terminal antisense nucleotide; 2' carbon modifications of the first and second or first, second, and third 5' terminal antisense nucleotides; and optionally 2' carbon modifications of the first and second or first, second, and third 5' terminal sense nucleotide. Control and exaequo molecules are also provided. siRNA molecules and related control, trackability and exaequo agents with specific stability modifications were developed.



GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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